UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/076,727	02/13/2002	John T. Groves	IB-1695	2093

8076 7590 02/03/2005

LAWRENCE BERKELEY NATIONAL LABORATORY
ONE CYCLOTRON ROAD, MAIL STOP 90B
UNIVERSITY OF CALIFORNIA
BERKELEY, CA 94720

EXAMINER	
SHIBUYA, MARK LANCE	

ART UNIT	PAPER NUMBER
1639	

DATE MAILED: 02/03/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/076,727	GROVES ET AL.	
	Examiner	Art Unit	
	Mark L. Shibuya	1639	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *11/24/2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-24* is/are pending in the application.

4a) Of the above claim(s) *1-6 and 21-24* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *7-20* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *5/15/02*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. Claims 1-24 are pending. Claims 1-6 and 21-24 are withdrawn from consideration. Claims 7-20 are examined.

Election/Restrictions

2. Applicant's election with traverse of Group II, claims 7-20, and the species that are cell adhesion protein dopant molecules that are cell adhesion proteins from the immunoglobulin superfamily and the species of phosphatidylserine, in the reply filed on 11/24/2004, is acknowledged. The traversal is on the ground(s) that the restriction between elected methods of Group II and the micro-array device of Group I is based on the examiner's reasoning that the micro-array device can be used to culture cells. Applicant argues that the micro-array devices of Group I have lipid membranes in each corral, and not cells; and states that there is no claim element describing cell culture. Applicant cites MPEP 806.05(g) that the examiner must provide material differences between process and apparatus.

This is not found persuasive because the specification as filed discloses that the product of Group I may be used to culture cells. The specification at para [0078], for example, states that cells may be cultured on the membranes of the claimed device. Claim 1 is drawn to a micro-array device for determining adherence of selected cells and claims lipid membranes in corrals for moving a plurality of cells. The Requirement for Restriction/Election, mailed 6/30/2004, states that Groups II and I are related as process and apparatus for its practice. The inventions of Groups II and I are distinct because the apparatus as claimed can be used to practice another and materially

different process. See MPEP 806.05(e). This is clear from the specification at para [0078], which discloses the separate uses of the product for cell culture and for cell adhesion products. Applicant's citation to MPEP 806.05(g) is misplaced because said MPEP section concerns apparatus and product made, whereas the instant traversal concerns Inventions related as process and apparatus for its practice.

The requirement is still deemed proper and is therefore made FINAL.

3. Claims 1-6 and 21-24 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in the reply filed on 11/24/2004.

Priority

4. This application claims benefit of 60/269,625, filed 2/16/2001, and claims benefit of 60/296,952, filed 6/8/2001.

Information Disclosure Statement

5. The information disclosure statement (IDS), filed 5/15/2002, has been considered.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> **The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.**

6. Claims 7, 13 and 15-20 rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 7 recites the language "a micro-array comprising an array of adjacent membrane corrals, membrane lipids and positively or negatively charged lipids", which renders the claim vague and indefinite, because it is unclear as to whether the three elements, separately, comprise a micro-array, or whether the three elements are in a defined relationship, such as adjacent membrane corrals, which contain membrane lipids, wherein the lipids are positively or negatively charged lipids. Alternatively, for example, the membrane lipids may be outside of the corrals and contain additional, exogenous positively or negatively charged lipids.

Claim 13 recites the limitation "the lipid" in line 1. There is uncertain antecedent basis for this limitation in the claim. It is unclear as to whether said lipid is of the "lipid bilayer membranes" (as in claim 8) or of "negatively or positively charged lipids" (as in claim 9).

Claim 15, and its dependent claims, recites the limitation "the membrane composition elements" in lines 1-2. There is insufficient antecedent basis for this limitation in the claim. Claim 15, and its dependent claims, recites the language "many membrane elements", where the term "many" is not defined by the claims or specification, so that one of skill in the art would not be reasonably apprised of the metes and bounds of the claimed invention.

Claim 16, and its dependent claims, recites the limitation "the membrane elements" in line 1. There is insufficient antecedent basis for this limitation in the claim.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

7. Claims 7-20 are rejected under 35 U.S.C. 102(e) as being anticipated by Kam et al., U.S. Publication No. 2002/0009807.

The claims are drawn to methods for screening, determining or observing living cell adhesion comprising providing a micro-array device comprising membranes in corrals, contacting or culturing cells in the device, and determining adhesion of the cells to the membranes; and wherein the membranes are lipid bilayers, wherein the membranes are doped with negatively or positively charged lipids, wherein the membranes are separated from a solid substrate by a water layer, wherein the substrate is a micropatterned glass wafer; wherein the membrane is an egg-phosphatidylcholine membrane; and wherein the lipid is phosphatidylserine (elected species).

Kam et al., U.S. Publication No. 2002/0009807, throughout publication, and at para [0027] teach methods for detecting cell adhesion using lipid bilayers separated from a solid support by a layer of water several nanometers thick, so that molecular components in the lipid bilayers of appropriate composition freely diffuse within the

plane of the membrane; at para [0029]-[0031], teach methods for micropatterning lipid bilayers in devices that facilitate adhesion of anchorage-dependent cells onto fluid membranes and at para [0047], [0051], teach barrier regions on the surface that surround regions for cell-adherence, which are "corrals" measuring 10 micrometer or 20 micrometer in width, but not 40 microns in width, so that cells may randomly sample membrane "elements" before adhering to one and that would prevent diffusion between the membranes of distinct corrals; at para [0061-[0062], teach cell adhesion experiments wherein cow pulmonary arterial endothelial cells were allowed to adhere for 6 hours to substrates with arrays of lipid corrals; at para [0030], [0058] teach devices having a plurality of distinct bilayer-compatible surface regions composed of different materials, and separated by one or more bilayer barrier regions and micropattern geometries in a regular array of squares measuring either 5, 10, 20, 40 micrometers in width (which reads on microarrays); at [0047], wherein the substrate is glass; at para [0040], at para [0048], teach membranes of bilayers of egg phosphatidylcholine and, at [0060] teach egg phosphatidylcholine membranes supplemented with a negatively charged phospholipid that is Texas Redo 1,2-dihexadecanoyl-sn-glycero-3-phosphoethanolamine (TR-PE).

8. Claims 7, 8, 14, 15, and 16 are rejected under 35 U.S.C. 102(e) as being anticipated by Chen et al., US Publication No. 2002/0182633.

The claims are drawn to methods for screening, determining or observing living cell adhesion comprising providing a micro-array device comprising membranes in

corrals, contacting or culturing cells in the device, and determining adhesion of the cells to the membranes; and wherein the membranes are lipid bilayers and wherein the device comprise corrals.

Chen et al., U.S. Publication No. 2002/0182633, throughout the publication, and especially at para [0012], at teach methods of observing and screening cell adhesivity or attachment, comprising biomolecules, including lipids, (specification at para [0022], [0066]) on glass substrates for use in microarray analysis; at para [0073] wherein the spatially patterned surfaces have areas that are adhesive to cells and areas that do not bind cells, and wherein the cell adhesive areas form islands that are isolated by cytophobic regions to which cells do not adhere (reading on corrals separated by barrier) and wherein the islands may have a lateral dimension of between 0.2 and 10 microns; at para [0102], teach lipid bilayers; at para [0109] teach allowing cells to attach for 2 hours; at para [0123] teach the visual assays for determining cell adhesion; and at para [0119] teach using glass wafers as supports.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was

not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

9. Claims 7-20 are rejected under 35 U.S.C. 103(a) as being unpatentable over Chen et al., U.S. Publication No. 2002/0182633 and Boxer et al., U.S. Patent No. 6,228,326. (IDS filed 5/15/2002).

The claims are drawn to methods for screening, determining or observing living cell adhesion comprising providing a micro-array device comprising membranes in corrals, contacting or culturing cells in the device, and determining adhesion of the cells to the membranes; and wherein the membranes are lipid bilayers, wherein the membranes are posed with negatively or positively charged lipids, wherein the membranes are separated from a solid substrate by a later layer, wherein the substrate is a micropatterned glass wafer; wherein the membrane is an egg-phosphatidylcholine membrane; wherein the lipid is phosphatidylserine (elected species).

Chen et al., U.S. Publication No. 2002/0182633, throughout the publication, and especially at para [0012], at teach methods of observing and screening cell adhesivity or attachment, comprising biomolecules, including lipids, (specification at para [0022], [0066]) on glass substrates for use in microarray analysis; at para [0073] wherein the spatially patterned surfaces have areas that are adhesive to cells and areas that do not bind cells, and wherein the cell adhesive areas form islands that are isolated by cytophobic regions to which cells do not adhere (reading on corrals and barriers) and wherein the islands may have a lateral dimension of between 0.2 and 10 microns; at para [0102], teach lipid bilayers; at para [0109] teach allowing cells to attach for 2 hours;

at para [0123] teach the visual assays for determining cell adhesion; and at para [0119] teach using glass wafers as supports.

The reference of Chen et al., does not disclose methods wherein the membranes of the micro-array are doped with negatively or positively charged lipids, the solid substrate is separated from the membranes by a water layer, wherein the membrane is an egg-phosphatidylcholine membrane; wherein the membrane comprises a lipid that is phosphatidylserine (elected species).

Boxer et al., U.S. Patent No. 6,228,326, throughout the patent and especially at col. 3, lines 28-col. 4, line 43, and col. 7, lines 50-61, teach devices having a surface defining a plurality of distinct bilayer-compatible surface regions separated by bilayer barrier regions that are corrals, and wherein the bilayers are carried on an aqueous film between the surface and the lipid bilayer; wherein the lipid bilayer expanse comprises phosphatidylserine and phosphatidylcholine; wherein the bilayer surface; at col. 8, lines 11-col. 53, teach support material microfabricated from a wafer of silicon, and wherein corrals are 5 micron square corrals; at col. 8, line 61-col. 9, line 20, teach egg phosphatidylcholine- cholesterol vesicles for preparing lipid bilayers via vesicle fusion; at col. 20, lines 15-21, teach egg phosphatidylcholine, and the fluorescent probe N-(Texas Red sulfonyl)-1,2-dihexadecanoyl-sn-glycero-3-phosphoethanolamine, triethylammonium salt. Boxer et al., at col. 21, lines 56-67, teach barriers to lateral diffusion, preventing mixing between fluid membranes in separate corrals.

It would have been prima facie obvious at the time the invention was made for one of ordinary skill in the are to have used methods of screening or

determining cell adhesion, wherein the membranes of the micro-array are doped with negatively or positively charged lipids, the solid substrate is separated from the membranes by a water layer, wherein the membrane is an egg-phosphatidylcholine membrane; and wherein the membrane comprises a lipid that is phosphatidylserine.

One of ordinary skill in the art would have been motivated to use methods for screening or determining cell adhesion because Chen et al. teach using methods for determining cell adhesion in order to control cell-surface interactions; and because Boxer et al. teach doping cell membranes with negatively charged, fluorescent lipids as markers to characterize the fluidity of membranes; because Boxer et al. teach membranes that are separated from the solid support by a water layer are produced by using fusion of vesicles to form lipid bilayer membranes, as taught in the art; membranes that are egg-phosphatidylcholine are long known in the art as a component for artificial lipid bilayer membranes; and membranes comprising phosphatidylserine because phosphatidylserine is a lipid well known for synthetic and natural vesicles.

One of ordinary skill in the arts would have had a reasonable expectation of success in using methods used methods of screening or determining cell adhesion, wherein the membranes of the micro-array are doped with negatively or positively charged lipids, the solid substrate is separated from the membranes by a water layer, wherein the membrane is an egg-phosphatidylcholine membrane; and wherein the membrane comprises a lipid that is phosphatidylserine, because artificial membranes doped with charged lipids, natural membranes containing egg-phosphatidylcholine and

synthetic or natural membranes comprising the lipid phosphatidylserine represent standard technologies that are well known in the art.

Conclusion

10. Claims 7-20 are rejected. Claims 1-6 and 21-24 are withdrawn.

11. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Mark L. Shibuya whose telephone number is (571) 272-0806. The examiner can normally be reached on M-F, 8:30AM-5:00PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Andrew Wang can be reached on (571) 272-0811. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Mark L. Shibuya
Examiner
Art Unit 1639

ms